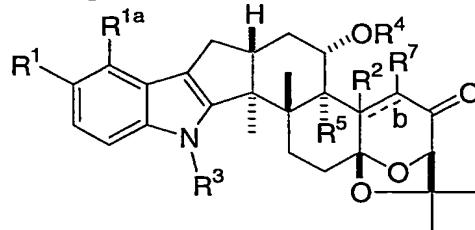


WHAT IS CLAIMED IS:

1. A compound of structural formula I:

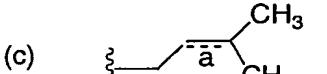
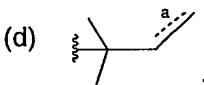


5

I

or a pharmaceutically acceptable salt, enantiomer, diastereomer, tautomer or mixture thereof, wherein,

R¹ and R^{1a} independently are:

10 (a) H,
 (b) C₁₋₆ alkyl
 (c)  , or
 (d)  ;

15 R² is:

(a) CO₂C₁₋₆alkyl,
 (b) H,
 (c) OH, or
 (d) C₁₋₆alkyl,

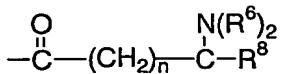
20 when a double bond is not present at b;

R³ is:

(a) H,
 (b) (C=O)OC₁₋₆alkyl or
 (c) C₁₋₆alkyl optionally substituted with OH, N(R⁶)₂, or CO₂R⁶;

R⁴ is

(a) H, provided that R³ is not H,
 (b) C₁₋₆alkyl optionally substituted with OH, N(R⁶)₂, or CO₂R⁶ or



5 (d) $\begin{array}{c} \text{O} \\ \parallel \\ \text{C}-\text{NH}(\text{CH}_2\text{)}_n\text{N}(\text{R}^6)_2; \end{array}$

R⁵ is:

(a) H,
 (b) OH, or
 10 (c) OC₁₋₆alkyl;

R⁶ is:

(a) H, or
 (b) C₁₋₆alkyl;

15

R⁷ is H, or C₁₋₆alkyl optionally substituted with OH, N(R⁶)₂, or CO₂R⁶;

20 R⁸ is H, C₁₋₆alkyl, CH₂-phenyl, CH₂-hydroxyphenyl, CH₂-indolyl, CH₂-imidazolyl, CH₂OR⁶, CH(OR⁶)CH₃, (CH₂)_nC(O)NR⁶, (CH₂)_nCO₂R⁶, (CH₂)_nSR⁶, (CH₂)_n(N⁺R⁶)₃,

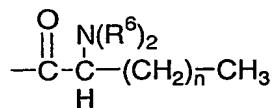
n is 0-4, and

— is a double bond optionally and independently present at a or b.

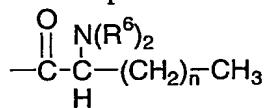
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2. A compound according to claim 1 wherein R¹, R^{1a} and R³ are hydrogen.

3. A compound according to claim 1 wherein R⁴ is

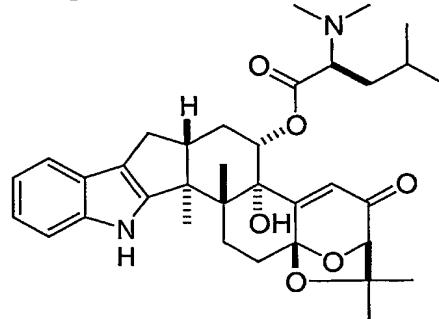


4. A compound according to claim 1 wherein R² and R⁷ are



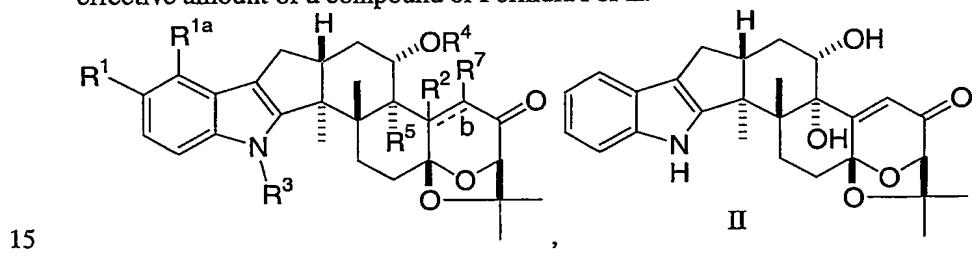
5 hydrogen and R⁴ is

5. A compound which is :



or a pharmaceutically acceptable salt, enantiomer, diastereomer, tautomer or mixture thereof.

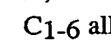
6. A method for treating ocular hypertension or glaucoma which comprises administering to a patient in need of such treatment a therapeutically effective amount of a compound of Formula I or II:



or a pharmaceutically acceptable salt, enantiomer, diastereomer, tautomer or mixture thereof:

wherein,

R^1 and R^{1a} independently are:

5 (a) H,
 (b) C₁₋₆ alkyl
 (c) 
 (d) 

R^2 is:

10 (a) $\text{CO}_2\text{C}_1\text{-6alkyl}$,
 (b) H,
 (c) OH, or
 (d) $\text{C}_1\text{-6alkyl}$,

when a double bond is not present at b;

15

\mathbb{R}^3 is:

- (a) H,
- (b) (C=O)OC₁₋₆alkyl or
- (c) C₁₋₆alkyl optionally substituted with OH, N(R⁶)₂, or CO₂R⁶;

20

\mathbb{R}^4 is

(a) H,
 (b) C₁₋₆alkyl optionally substituted with OH, N(R⁶)₂, or CO₂R⁶ or

$$\begin{array}{c} \text{O} \\ \parallel \\ \text{---C---}(\text{CH}_2)_n\text{---C---R}^8 \\ \text{(c)} \end{array} \quad \begin{array}{c} \text{N}(\text{R}^6)_2 \\ | \\ \text{H} \end{array} \quad \text{or}$$

25

(d) $\text{--C}(\text{H}_3)\text{--NH}(\text{CH}_2)_n\text{N}(\text{R}^6)_2$:

R⁵ is:

(a) H_1

- (b) OH, or
- (c) OC₁₋₆alkyl;

R⁶ is:

- 5 (a) H, or
- (b) C₁₋₆alkyl;

R⁷ is H, or C₁₋₆alkyl optionally substituted with OH, N(R⁶)₂, or CO₂R⁶;

10 R⁸ is H, C₁₋₆alkyl, CH₂-phenyl, CH₂-hydroxyphenyl, CH₂-indolyl, CH₂-imidazolyl, CH₂OR⁶, CH(OR⁶)CH₃, (CH₂)_nC(O)NR⁶, (CH₂)_nCO₂R⁶, (CH₂)_nSR⁶, (CH₂)_n(N⁺R⁶)₃,

n is 0-4 and

15 — is a double bond optionally and independently present at a or b.

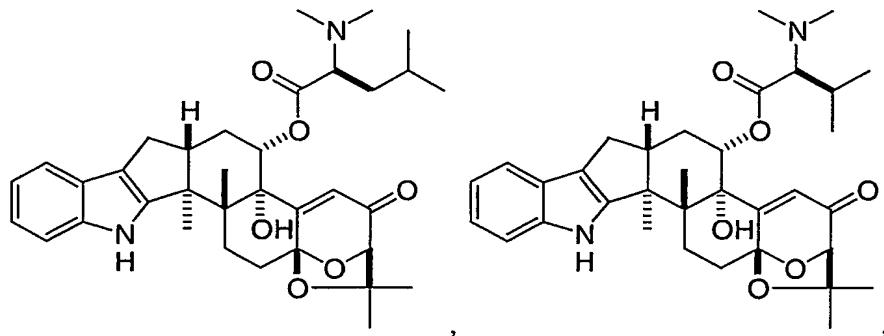
7. The method according to Claim 6 wherein the compound of formula I is applied as a topical formulation in the form of a solution or suspension.

20 8. The method of Claim 7, which comprises administering a second active ingredient, concurrently or consecutively, wherein the second active ingredient is a hypotensive agent selected from a β -adrenergic blocking agent, adrenergic agonist, a parasympathomimetic agent, a carbonic anhydrase inhibitor, an EP4 agonist and a prostaglandin or a prostaglandin derivative.

30 9. The method according to claim 8 wherein the β -adrenergic blocking agent is timolol, levobunolol, carteolol, optipranolol, metapranolol or betaxolol; the parasympathomimetic agent is pilocarpine, carbachol, or phospholine iodide; adrenergic agonist is iopidine, brimonidine, epinephrine, or dipivefrin, the carbonic anhydrase inhibitor is dorzolamide, acetazolamide, metazolamide or brinzolamide; the prostaglandin is latanoprost or rescula, and the prostaglandin derivative is a hypotensive lipid derived from PGF2 α prostaglandins.

10. A method according to claim 7 in which the topical formulation contains xanthan gum or gellan gum.

11. A method according to claim 6 wherein the compound of
5 formula I is:



or a pharmaceutically acceptable salt, enantiomer, diastereomer, tautomer or mixture thereof.

10

12. A method for treating macular edema, macular degeneration, or for providing a neuroprotective effect, which comprises administering to a patient in need of such treatment a pharmaceutically effective amount of a compound as recited in claim 6.

15

13. The method according to Claim 12 wherein the compound of formula I is applied as a topical formulation in the form of a solution or suspension.

20

14. The method of Claim 13, which comprises administering a second active ingredient, concurrently or consecutively, wherein the second active ingredient is a hypotensive agent selected from a β -adrenergic blocking agent, adrenergic agonist, a parasympathomimetic agent, a carbonic anhydrase inhibitor, an EP4 agonist and a prostaglandin or a prostaglandin derivative.

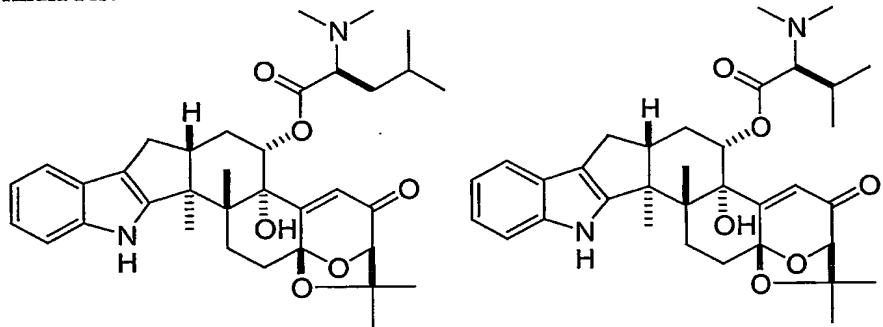
25

15. The method according to claim 14 wherein the β -adrenergic blocking agent is timolol, levobunolol, carteolol, optipranolol, metapranolol or betaxolol; the parasympathomimetic agent is pilocarpine, carbachol, or phospholine

iodide; adrenergic agonist is iopidine, brimonidine, epinephrine, or dipivephrin, the carbonic anhydrase inhibitor is dorzolamide, acetazolamide, metazolamide or brinzolamide; the prostaglandin is latanoprost or rescula, and the prostaglandin derivative is a hypotensive lipid derived from PGF2 α prostaglandins.

5 16. A method according to claim 12 in which the topical formulation contains xanthan gum or gellan gum.

17. A method according to claim 13 wherein the compound of formula I is:

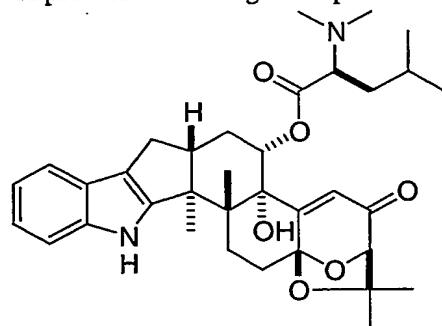


10

or a pharmaceutically acceptable salt, enantiomer, diastereomer, tautomer or mixture thereof.

15 18. A composition comprising a compound of formula I as recited in claim 1 and a pharmaceutically acceptable carrier.

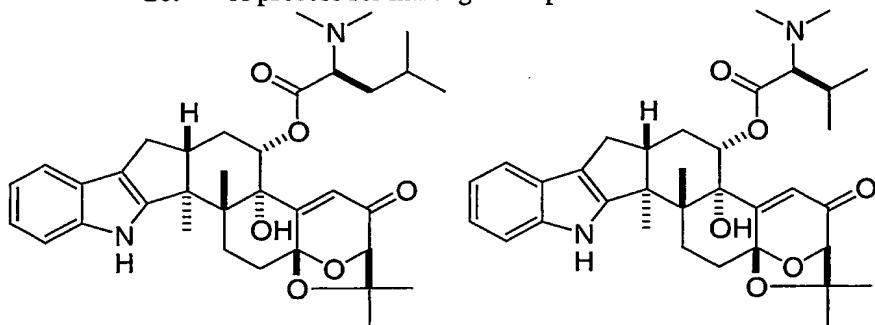
19. A process for making a compound of the formula Ia:



Ia

or a pharmaceutically acceptable salt, enantiomer, diastereomer, tautomer or
5 mixture thereof, using microbiological strain *Aspergillus alliaceus* (ATCC No.
Aspergillus nomius (ATCC No. 15546 or PTA-4211), or
Aspergillus nomius (ATCC No. PTA-4212).

20. A process for making a compound of the formula Ia or Ib:



10

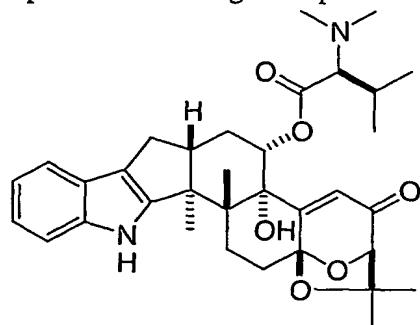
Ia

Ib

or a pharmaceutically acceptable salt, enantiomer, diastereomer, tautomer or
mixture thereof, using microbiological strain *Aspergillus nomius* ATCC No.
15546 (PTA-4211).

15

21. A process for making a compound of the formula Ib:



Ib

or a pharmaceutically acceptable salt, enantiomer, diastereomer, tautomer or
5 mixture thereof, using microbiological strain *Aspergillus nomius* ATCC No. PTA-
4212.